

REMARKS**I. Status of Claims**

Claims 1, 9-15, 18-38 and 40 are pending in the application. Claims 1, 9, 18-24, 27, 28, 34-38 and 40 are rejected under 35 U.S.C. §103 over Lehrer *et al.* The specific grounds for rejection, and applicants response thereto, are set out in detail below.

II. Rejection Under 35 U.S.C. §103

Claims 1, 8, 9, 18-24, 27, 28, 34-38 and 40 stand rejected as obvious over Lehrer *et al.* The office action states that a combination of Lehrer's SEQ ID NOS: 27 and 34 will give the sequence of the present application's SEQ ID NO:31, and that a combination of Lehrer's SEQ ID NOS: 18 and 34 will give the sequence of the present application's SEQ ID NO:32. The rejection is premised on the circularization of applicants' peptides. Applicants appreciate the examiner's clarification and restatement of the rejection, but nonetheless traverse.

The present invention is drawn to two specific peptides, SEQ ID NOS:31 and 32. The examiner recognizes this fact in that the rejection is being advanced under §103 and not §102, as these two peptides are nowhere disclosed in the Lehrer application. Thus, the reference is correctly characterized as teaching a genus of circular retrocyclin peptides comprising "two linked nonapeptides that maybe identical or different." Lehrer at page 7, lines 8-10. Lehrer sets forth 46 different nonapeptides (SEQ ID NOS:19-64) that may be combined to form a retrocyclin. Lehrer at pages 7-17 of the Sequence Listing. Thus, if peptide "A" may be one of 46 different nonapeptides, and peptide "B" selected from the same group, the number of members in this genus is 46 X 46, or 2116. The examiner has found, using applicants' claims as a searching point, that SEQ ID NOS:31 and 32 can be identified as members of the 2000+

peptide genus described by Lehrer, and applicants do not disagree. However, this is far short of what is needed to find obviousness in this situation.

"In determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having the reference before him to make the proposed substitution, combination, or other modification." *In re Linter*, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972). Obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

MPEP §2144.08, which is particularly instructive on this rejection, is entitled "Obviousness of Species When Prior Art Teaches Genus." According to that section of the MPEP, the analysis begins at the point during examination after a single prior art reference is found disclosing a genus encompassing the claimed species or subgenus. If the most relevant prior art consists of a single prior art reference disclosing a genus encompassing the claimed species, which appears to be the case here, examiner should follow the guidelines set forth therein.

Per this section, in order to determine whether the claimed species would have been obvious to one of ordinary skill in the art at the time the invention was made, the patentability of a claim to a specific compound(s) should be analyzed no differently than any other claim for purposes of §103, namely, by examining the scope and contents of the prior art, the differences between the prior art and the claims in issue, the level of skill in the pertinent art, and any

evidence of secondary considerations. In particular, the fact that a claimed species is encompassed by a prior art genus is not sufficient by itself to establish a *prima facie* case of obviousness. *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994) (“The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious.”); *In re Jones*, 958 F.2d 347, 350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992) (Federal Circuit has “decline[d] to extract from *Merck [& Co. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir. 1989)] the rule that... regardless of how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it.”). See also *In re Deuel*, 51 F.3d 1552, 1559, 34 USPQ2d 1210, 1215 (Fed. Cir. 1995).

To establish a *prima facie* case of obviousness in a genus-species chemical composition situation, it is essential that examiner find some motivation or suggestion to make the claimed invention in light of the prior art teachings. See, e.g., *In re Brouwer*, 77 F.3d 422, 425, 37 USPQ2d 1663, 1666 (Fed. Cir. 1996) (“[T]he mere possibility that one of the esters or the active methylene group-containing compounds... could be modified or replaced such that its use would lead to the specific sulfoalkylated resin recited in claim 8 does not make the process recited in claim 8 obvious ‘unless the prior art suggested the desirability of [such a] modification’ or replacement.”) (quoting *In re Gordon*, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984)); *In re Vaeck*, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991) (“[A] proper analysis under §103 requires, *inter alia*, consideration of ... whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process.”). **Regardless of the type of disclosure**, the prior art must provide some motivation to one of ordinary skill in the art to make the claimed invention in order to support a conclusion of obviousness. See, e.g., *Vaeck*, 947 F.2d at 493, 20

USPQ2d at 1442 (A proper obviousness analysis requires consideration of “whether the prior art would also have revealed that in so making or carrying out [the claimed invention], those of ordinary skill would have a reasonable expectation of success.”); *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988) (“The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art.”); *Hodosh v. Block Drug Co.*, 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986).

In the case of a prior art reference disclosing a genus, the examiner should make findings as to:

- (A) the structure of the disclosed prior art genus and that of any expressly described species or subgenus within the genus;
- (B) any physical or chemical properties and utilities disclosed for the genus, as well as any suggested limitations on the usefulness of the genus, and any problems alleged to be addressed by the genus;
- (C) the predictability of the technology; and
- (D) the number of species encompassed by the genus taking into consideration all of the variables possible.

As discussed above, the question boils down to whether one of ordinary skill in the relevant art would have been motivated to select the claimed species from the disclosed prior art genus. See, e.g., *Ochiai*, 71 F.3d at 1569-70, 37 USPQ2d at 1131; *Deuel*, 51 F.3d at 1557, 34 USPQ2d at 1214 (“[A] *prima facie* case of unpatentability requires that the teachings of the prior art suggest *the claimed compounds* to a person of ordinary skill in the art” (emphasis in original)); *Jones*, 958 F.2d at 351, 21 USPQ2d at 1943-44 (Fed. Cir. 1992); *Dillon*, 919 F.2d at 692, 16 USPQ2d at 1901; *In re Lahu*, 747 F.2d 703, 705, 223 USPQ 1257, 1258 (Fed. Cir. 1984) (“The prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular

modifications needed to arrive at the claimed compound.”). See also *In re Kemps*, 97 F.3d 1427, 1430, 40 USPQ2d 1309, 1311 (Fed. Cir. 1996) (discussing motivation to combine). The following discussion presents the U.S. PTO’s stringent requirements for such an analysis.

First, the PTO must consider the size of the prior art genus, bearing in mind that size alone cannot support an obviousness rejection. See, e.g., *Baird*, 16 F.3d at 383, 29 USPQ2d at 1552 (observing that “it is not the mere number of compounds in this limited class which is significant here but, rather, the total circumstances involved”). While there is no absolute correlation between the size of the prior art genus and a conclusion of obviousness, even a small number of genus members cannot itself create a *per se* rule of obviousness in the absence of *some* motivation to select the claimed species. See, e.g., *Deuel*, 51 F.3d at 1558-59, 34 USPQ2d at 1215 (“No particular one of these DNAs can be obvious unless there is something in the prior art to lead to the particular DNA and indicate that it should be prepared.”); *Baird*, 16 F.3d at 382-83, 29 USPQ2d at 1552; *Bell*, 991 F.2d at 784, 26 USPQ2d at 1531 (“Absent anything in the cited prior art suggesting which of the 10^{36} possible sequences suggested by Rinderknecht corresponds to the IGF gene, the PTO has not met its burden of establishing that the prior art would have suggested the claimed sequences.”); *In re Ruschig*, 343 F.2d 965, 974, 145 USPQ 274, 282 (CCPA 1965) (Rejection of claimed compound in light of prior art genus based on *Petering* is not appropriate where the prior art does not disclose a small recognizable class of compounds with common properties.). Here, there is a large genus, and more importantly, no discussion of why the claimed species would have been selected.

Other relevant factors noticeably overlooked in the action are the number of variables which must be selected or modified, and the nature and significance of the differences between the prior art and the claimed invention. See, e.g., *In re Jones*, 958 F.2d 347, 350, 21 USPQ2d

1941, 1943 (Fed. Cir. 1992) (reversing obviousness rejection of novel dicamba salt with acyclic structure over broad prior art genus encompassing claimed salt, where disclosed examples of genus were dissimilar in structure, lacking an ether linkage or being cyclic); *In re Susi*, 440 F.2d 442, 445, 169 USPQ 423, 425 (CCPA 1971) (the difference from the particularly preferred subgenus of the prior art was a hydroxyl group, a difference conceded by applicant "to be of little importance"). In the area of biotechnology, of which the present invention is an example, an exemplified species may differ from a claimed species by a conservative or non-conservative substitution, although at some locations even a conservative substitution may not be permitted. For example, the gain or loss of even one methyl group can destabilize the structure if close packing is required in the interior of domains. James Darnell *et al.*, *Molecular Cell Biology* 51 (2d ed. 1990).

Also relevant, and notably unaddressed in the action, is the general predictability of the technology. See, *e.g.*, *Dillon*, 919 F.2d at 692-97, 16 USPQ2d at 1901-05; *In re Grabiak*, 769 F.2d 729, 732-33, 226 USPQ 870, 872 (Fed. Cir. 1985). If the technology is unpredictable, it is less likely that structurally similar species will render a claimed species obvious because it may not be reasonable to infer that they would share similar properties. See, *e.g.*, *In re May*, 574 F.2d 1082, 1094, 197 USPQ 601, 611 (CCPA 1978) (*prima facie* obviousness of claimed analgesic compound based on structurally similar prior art isomer was rebutted with evidence demonstrating that analgesia and addiction properties could not be reliably predicted on the basis of chemical structure); *In re Schechter*, 205 F.2d 185, 191, 98 USPQ 144, 150 (CCPA 1953) (unpredictability in the insecticide field, with homologs, isomers and analogs of known effective insecticides having proven ineffective as insecticides, was considered as a factor weighing against a conclusion of obviousness of the claimed compounds). However, obviousness does not

require absolute predictability, only a reasonable expectation of success, *i.e.*, a reasonable expectation of obtaining similar properties. See, *e.g.*, *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). Here, the PTO will no doubt agree that the technologic area – inhibition of HIV – is an unpredictable endeavor.

In sum, based on the foregoing factors and the evidence as a whole (*In re Bell*, 991 F.2d 781,784, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993); *In re Kulling*, 897 F.2d 1147, 1149, 14 USPQ2d 1056, 1057 (Fed. Cir. 1990)), the examiner should make express fact-findings relating to the *Graham* factors and address the issues set forth above. The fact-findings should specifically articulate what teachings or suggestions in the prior art would have motivated one of ordinary skill in the art to select the claimed species. *Kulling*, 897 F.2d at 1149, 14 USPQ2d at 1058; *Panduit Corp. v. Dennison Mfg. Co.*, 810 F.2d 1561, 1579 n.42, 1 USPQ2d 1593, 1606 n.42 (Fed. Cir. 1987). Only then can it be determined whether these findings, considered as a whole, support a *prima facie* case that the claimed invention would have been obvious to one of ordinary skill in the relevant art at the time the invention was made. However, here the action does no more than establish that the claimed species fall within the genus described by Lehrer, and does not address any of the factors set out above that would otherwise support the rejection. Thus, it is respectfully submitted that the rejection is improper on its face and does not establish *prima facie* obviousness. Reconsideration and withdrawal of the rejection is therefore requested.

III. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance and an early notification to that effect is earnestly solicited. Should the examiner have any questions regarding this response

Respectfully submitted,



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